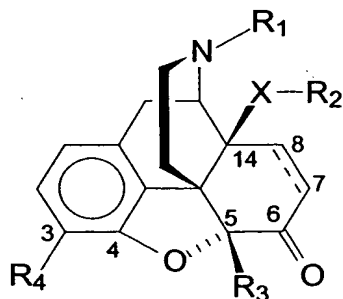
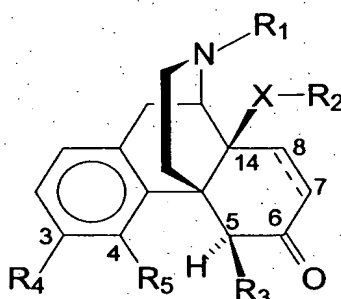


# Claims

- Compounds of the formula (I) or (Ia),



(I)



(Ia)

in which the substituents have the following significance:

R<sub>1</sub>: C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyl, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyl, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyl, where alkinyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinyl is C<sub>2</sub>-C<sub>6</sub>-alkinyl;

R<sub>2</sub>: subject to the following definition of X, hydrogen, C<sub>4</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyl, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyl, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyl, where alkinyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinyl is C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>6</sub>-alkenoyl; C<sub>3</sub>-C<sub>6</sub>-alkinoyl; C<sub>9</sub>-C<sub>16</sub>-arylalkenoyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenoyl is C<sub>3</sub>-C<sub>6</sub>-alkenoyl; C<sub>9</sub>-C<sub>16</sub>-arylalkinoyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinoyl is C<sub>3</sub>-C<sub>6</sub>-alkinoyl;

R<sub>3</sub>: hydrogen; C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; alkoxyalkyl, where alkoxy is C<sub>1</sub>-C<sub>6</sub>-alkoxy and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; CO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub>-alkyl); CO<sub>2</sub>H; CH<sub>2</sub>OH.

R<sub>4</sub>: hydrogen; hydroxy; C<sub>1</sub>-C<sub>6</sub>-alkyloxy; C<sub>2</sub>-C<sub>10</sub>-alkyloxyalkoxy, where alkyloxy is C<sub>1</sub>-C<sub>4</sub> and alkoxy is C<sub>1</sub>-C<sub>6</sub>-alkyloxy; C<sub>2</sub>-C<sub>6</sub>-alkenyloxy; C<sub>2</sub>-C<sub>6</sub>-alkinyloxy; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyloxy, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyloxy, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical

saturated group)alkinyloxy where alkynyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkynyl is C<sub>2</sub>-C<sub>6</sub>-alkynyl; C<sub>1</sub>-C<sub>6</sub>-alkanoyloxy; C<sub>3</sub>-C<sub>6</sub>-alkenoyloxy; C<sub>3</sub>-C<sub>6</sub>-alkinoyloxy; C<sub>7</sub>-C<sub>16</sub>-arylalkanoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkanoyloxy is C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy; C<sub>9</sub>-C<sub>16</sub>-arylalkenoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenoyloxy is C<sub>3</sub>-C<sub>6</sub>-alkenoyloxy; C<sub>9</sub>-C<sub>16</sub>-arylalkinoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinoyloxy is C<sub>3</sub>-C<sub>6</sub>-alkinoyloxy;

R<sub>5</sub>: hydrogen; hydroxy; C<sub>1</sub>-C<sub>6</sub>-alkyloxy; C<sub>2</sub>-C<sub>10</sub>-alkyloxyalkoxy, where alkyloxy is C<sub>1</sub>-C<sub>4</sub> and alkoxy is C<sub>1</sub>-C<sub>6</sub>-alkyloxy; C<sub>2</sub>-C<sub>6</sub>-alkenyloxy; C<sub>2</sub>-C<sub>6</sub>-alkinyloxy; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyloxy, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyloxy, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyloxy, where alkynyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkynyl is C<sub>2</sub>-C<sub>6</sub>-alkynyl; C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy; C<sub>7</sub>-C<sub>16</sub>-arylalkanoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkanoyloxy is C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy;

X is oxygen, sulphur or methylene;

wherein a single or double bond can be present between the carbon atoms of numbers 7 and 8,

wherein alkyl, alkenyl and alkynyl can each be branched or unbranched, aryl can be unsubstituted or mono-, di- or trisubstituted, independently in each case, with hydroxy, halogen, nitro, cyano, thiocyanato, trifluoromethyl, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy, CO<sub>2</sub>H, CONH<sub>2</sub>, CO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>-alkyl), CONH(C<sub>1</sub>-C<sub>3</sub>-alkyl), CON(C<sub>1</sub>-C<sub>3</sub>-alkyl)<sub>2</sub>, CO(C<sub>1</sub>-C<sub>3</sub>-alkyl); amino; (C<sub>1</sub>-C<sub>3</sub>-monoalkyl)amino, (C<sub>1</sub>-C<sub>3</sub>-dialkyl)amino; C<sub>5</sub>-C<sub>6</sub>-cycloalkylamino, (C<sub>1</sub>-C<sub>3</sub>-alkanoyl)amido, SH, SO<sub>3</sub>H, SO<sub>3</sub>(C<sub>1</sub>-C<sub>3</sub>-alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>-alkyl), SO(C<sub>1</sub>-C<sub>3</sub>-alkyl), C<sub>1</sub>-C<sub>3</sub>-alkylthio or C<sub>1</sub>-C<sub>3</sub>-alkanoylthio,

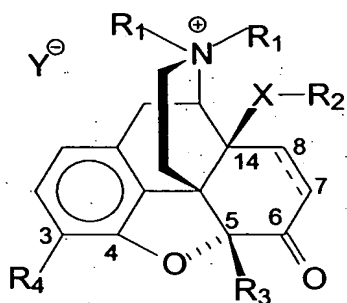
wherein -(cyclical saturated group) is either preferably C<sub>3</sub>-C<sub>10</sub>-cycloalkyl or a heterocyclical group with 2 to 9 carbon atoms, containing further one or more heteroatoms,

**with the exception of compounds** where R<sub>1</sub> is methyl, R<sub>2</sub> is C<sub>4</sub>-C<sub>6</sub>-alkyl, R<sub>3</sub> is hydrogen or methyl, R<sub>4</sub> is hydroxy or methoxy and R<sub>5</sub> is hydroxy, methoxy or an oxygen atom bound to the carbon atom in the 5<sup>th</sup> position, when X is oxygen;

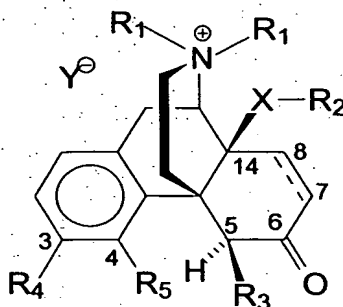
**with the further exception of compounds** where R<sub>1</sub> is cyclopropylmethyl and XR<sub>2</sub> is benzyloxy, when R<sub>4</sub> is oxygen or benzyloxy and R<sub>5</sub> is an oxygen atom bound to the carbon atom in the 5<sup>th</sup> position;

**with the further exception of compounds** where R<sub>1</sub> is cyclopropylmethyl and XR<sub>2</sub> is benzyloxy, when R<sub>4</sub> is oxygen, hydroxy or benzyloxy and R<sub>5</sub> is hydroxy or methoxy.

## 2. Compounds of the formula (IA) or (IAa),



(IA)



(IAa)

where the substituents have the following significance:

$R_1$ :  $C_1$ - $C_6$ -alkyl;  $C_2$ - $C_6$ -alkenyl;  $C_2$ - $C_6$ -alkinyl;  $C_3$ - $C_{16}$ -(cyclical saturated group)alkyl, where alkyl is  $C_1$ - $C_6$ ;  $C_4$ - $C_{16}$ -(cyclical saturated group)alkenyl, where alkenyl is  $C_2$ - $C_6$ ;  $C_4$ - $C_{16}$ -(cyclical saturated group)alkinyl, where alkinyl is  $C_2$ - $C_6$ ;  $C_7$ - $C_{16}$ -arylalkyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkyl is  $C_1$ - $C_6$ -alkyl;  $C_8$ - $C_{16}$ -arylalkenyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkenyl is  $C_2$ - $C_6$ -alkenyl;  $C_8$ - $C_{16}$ -arylalkinyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkinyl is  $C_2$ - $C_6$ -alkinyl;

wherein the two substituents  $R_1$  can be the same or different;

$R_2$ : subject to the following definition of X, hydrogen,  $C_1$ - $C_6$ -alkyl;  $C_2$ - $C_6$ -alkenyl;  $C_2$ - $C_6$ -alkinyl;  $C_3$ - $C_{16}$ -(cyclical saturated group)alkyl, where alkyl is  $C_1$ - $C_6$ ;  $C_4$ - $C_{16}$ -(cyclical saturated group)alkenyl, where alkenyl is  $C_2$ - $C_6$ ;  $C_4$ - $C_{16}$ -(cyclical saturated group)alkinyl, where alkinyl is  $C_2$ - $C_6$ ;  $C_7$ - $C_{16}$ -arylalkyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkyl is  $C_1$ - $C_6$ -alkyl;  $C_8$ - $C_{16}$ -arylalkenyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkenyl is  $C_2$ - $C_6$ -alkenyl;  $C_8$ - $C_{16}$ -arylalkinyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkinyl is  $C_2$ - $C_6$ -alkinyl;  $C_2$ - $C_6$ -alkanoyl;  $C_3$ - $C_6$ -alkenoyl;  $C_3$ - $C_6$ -alkinoyl;  $C_8$ - $C_{16}$ -arylalkanoyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkanoyl is  $C_2$ - $C_6$ -alkyl;  $C_9$ - $C_{16}$ -arylalkenoyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkenoyl is  $C_3$ - $C_6$ -alkenoyl;  $C_9$ - $C_{16}$ -arylalkinoyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkinoyl is  $C_3$ - $C_6$ -alkinoyl;

$R_3$ : hydrogen;  $C_1$ - $C_6$ -alkyl;  $C_2$ - $C_6$ -alkenyl;  $C_7$ - $C_{16}$ -arylalkyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkyl is  $C_1$ - $C_6$ -alkyl;  $C_8$ - $C_{16}$ -arylalkenyl, where aryl is  $C_6$ - $C_{10}$ -aryl and alkenyl is  $C_2$ - $C_6$ -alkenyl; alkoxyalkyl, where alkoxy is  $C_1$ - $C_6$ -alkoxy and alkyl is  $C_1$ - $C_6$ -alkyl;  $CO_2(C_1$ - $C_6$ -alkyl);  $CO_2H$ ;  $CH_2OH$ .

$R_4$ : hydrogen; hydroxy;  $C_1$ - $C_6$ -alkyloxy;  $C_2$ - $C_{10}$ -alkyloxyalkoxy, where alkyloxy is  $C_1$ - $C_4$  and alkoxy is  $C_1$ - $C_6$ -alkyloxy;  $C_2$ - $C_6$ -alkenyloxy;  $C_2$ - $C_6$ -alkinyloxy;  $C_3$ - $C_{16}$ -(cyclical saturated group)alkyloxy, where alkyl is  $C_1$ - $C_6$ ;  $C_4$ - $C_{16}$ -(cyclical saturated group)alkenyloxy, where alkenyl is  $C_2$ - $C_6$ ;  $C_4$ - $C_{16}$ -(cyclical

saturated group)alkinyloxy where alkynyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkynyl is C<sub>2</sub>-C<sub>6</sub>-alkynyl; C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy; C<sub>3</sub>-C<sub>6</sub>-alkenoyloxy; C<sub>3</sub>-C<sub>6</sub>-alkinoyloxy; C<sub>8</sub>-C<sub>16</sub>-arylalkanoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkanoyloxy is C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy; C<sub>9</sub>-C<sub>16</sub>-arylalkenoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenoyloxy is C<sub>3</sub>-C<sub>6</sub>-alkenoyloxy; C<sub>9</sub>-C<sub>16</sub>-arylalkinoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinoyloxy is C<sub>3</sub>-C<sub>6</sub>-alkinoyloxy;

R<sub>5</sub>: hydrogen; hydroxy; C<sub>1</sub>-C<sub>6</sub>-alkyloxy; C<sub>2</sub>-C<sub>10</sub>-alkyloxyalkoxy, where alkyloxy is C<sub>1</sub>-C<sub>4</sub> and alkoxy is C<sub>1</sub>-C<sub>6</sub>-alkyloxy; C<sub>2</sub>-C<sub>6</sub>-alkenyloxy; C<sub>2</sub>-C<sub>6</sub>-alkinyloxy; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyloxy, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyloxy, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyloxy, where alkynyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkynyl is C<sub>2</sub>-C<sub>6</sub>-alkynyl; C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy; C<sub>7</sub>-C<sub>16</sub>-arylalkanoyloxy, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkanoyloxy is C<sub>2</sub>-C<sub>6</sub>-alkanoyloxy;

X is oxygen, sulphur or methylene;

Y<sup>-</sup> is I<sup>-</sup>, Br<sup>-</sup>, Cl<sup>-</sup>, OH<sup>-</sup> or another pharmacologically acceptable counterion;

wherein a single or double bond can be present between the carbon atoms of numbers 7 and 8,

wherein alkyl, alkenyl and alkynyl can each be branched or unbranched, aryl can be unsubstituted or mono-, di- or trisubstituted, independently in each case, with hydroxy, halogen, nitro, cyano, thiocyanato, trifluoromethyl, C<sub>1</sub>-C<sub>3</sub>-alkyl, C<sub>1</sub>-C<sub>3</sub>-alkoxy, CO<sub>2</sub>H, CONH<sub>2</sub>, CO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>-alkyl), CONH(C<sub>1</sub>-C<sub>3</sub>-alkyl), CON(C<sub>1</sub>-C<sub>3</sub>-alkyl)<sub>2</sub>, CO(C<sub>1</sub>-C<sub>3</sub>-alkyl); amino; (C<sub>1</sub>-C<sub>3</sub>-monoalkyl)amino, (C<sub>1</sub>-C<sub>3</sub>-dialkyl)amino; C<sub>5</sub>-C<sub>6</sub>-cycloalkylamino, (C<sub>1</sub>-C<sub>3</sub>-alkanoyl)amido, SH, SO<sub>3</sub>H, SO<sub>3</sub>(C<sub>1</sub>-C<sub>3</sub>-alkyl), SO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>-alkyl), SO(C<sub>1</sub>-C<sub>3</sub>-alkyl), C<sub>1</sub>-C<sub>3</sub>-alkylthio or C<sub>1</sub>-C<sub>3</sub>-alkanoylthio,

wherein -(cyclical saturated group) is either preferably C<sub>3</sub>-C<sub>10</sub>-cycloalkyl or a heterocyclical group with 2 to 9 carbon atoms, containing furthermore one or more heteroatoms.

3. Compounds of the formulae (I) or (IA) of Claims 1 and 2, in which X is oxygen; R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>4</sub>-C<sub>16</sub>-cycloalkylalkyl, where cycloalkyl is C<sub>3</sub>-C<sub>10</sub> and alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; R<sub>2</sub> is C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; R<sub>3</sub> is hydrogen or methyl; R<sub>4</sub> is hydroxy, methoxy or acetoxy.

4. Compounds of the formula (IA) of Claim 2, in which X is oxygen; R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>4</sub>-C<sub>16</sub>-cycloalkylalkyl, where cycloalkyl is C<sub>3</sub>-C<sub>10</sub> and alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; R<sub>2</sub> is C<sub>1</sub>-C<sub>6</sub>-alkyl or C<sub>2</sub>-C<sub>6</sub>-alkenyl, R<sub>3</sub> is hydrogen or methyl; R<sub>4</sub> is hydroxy, methoxy or acetoxy.

5. Compounds of Claims 1 and 2, selected from:

17-allyl-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-allyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-allyl-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-allyl-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclobutylmethyl-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclobutylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclobutylmethyl-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclobutylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ ,17-dimethyl-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, 4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ ,17-dimethyl-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, 17-propyl-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-propyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-propyl-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-propyl-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-tetrahydrofurfuryl-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-tetrahydrofurfuryl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-tetrahydrofurfuryl-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-tetrahydrofurfuryl-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-(2-phenylethyl)-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-(2-phenylethyl)-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-(2-phenylethyl)-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-(2-phenylethyl)-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-ethyl-4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-ethyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-ethyl-4,5 $\alpha$ -epoxy-3-methoxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-ethyl-4,5 $\alpha$ -epoxy-3-hydroxy-5 $\beta$ -methyl-14 $\beta$ -(3-phenylpropyloxy)morphinan-6-one, 17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -[(2-

methylbenzyl)oxy]morphinan-6-one, 14 $\beta$ -[(2-chlorobenzyl)oxy]-17-(cyclopropylmethyl)-4,5 $\alpha$ -epoxy-3-hydroxymorphinan-6-one, 14 $\beta$ -benzyloxy-17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxymorphinan-6-one, 14 $\beta$ -butoxy-17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxymorphinan-6-one, 17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -[(3-methylbutyl)oxy]morphinan-6-one, 4,5 $\alpha$ -epoxy-5 $\beta$ ,17-dimethyl-14 $\beta$ -[(3-phenylpropyl)oxy]-3-[(prop-2-ynyl)oxy]morphinan-6-one, 14 $\beta$ -[(3-chlorobenzyl)oxy]-4,5 $\alpha$ -epoxy-17-methyl-3-[(prop-2-ynyl)oxy]morphinan-6-one, 4,5 $\alpha$ -epoxy-17-ethyl-3-methoxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, 4,5 $\alpha$ -epoxy-17-ethyl-3-hydroxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, 4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -[(3-methylbutyl)oxy]-17-propylmorphinan-6-one, 5 $\beta$ -benzyl-14-methoxycodeinone (= 5-benzyl-7,8-didehydro-4,5 $\alpha$ -epoxy-3,14 $\beta$ -dimethoxy-17-methyl-morphinan-6-one), 5 $\beta$ -benzyl-4,5 $\alpha$ -epoxy-3,14 $\beta$ -dimethoxy-17-methylmorphinan-6-one, 5 $\beta$ -benzyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -methoxy-17-methylmorphinan-6-one, 4-hydroxy-3-methoxy-17-methyl-14-[(3-phenylpropyl)oxy]-morphinan-6-one, 3,4-dimethoxy-17-methyl-14-[(3-phenylpropyl)oxy]-morphinan-6-one, 14 $\beta$ -benzyloxy-4-hydroxy-3-methoxy-17-methylmorphinan-6-one, 14 $\beta$ -benzyloxy-3,4-dimethoxy-17-methylmorphinan-6-one, 4-hydroxy-3-methoxy-17-methyl-14 $\beta$ -[(2-naphthylmethyl)oxy]morphinan-6-one, 3,4-dimethoxy-17-methyl-14 $\beta$ -[(2-naphthylmethyl)oxy]morphinan-6-one, 4-hydroxy-3-methoxy-5 $\beta$ ,17-dimethyl-14 $\beta$ -[(3-phenylpropyl)oxy]-morphinan-6-one, 3,4-dimethoxy-5 $\beta$ ,17-dimethyl-14 $\beta$ -[(3-phenylpropyl)oxy]-morphinan-6-one, 14 $\beta$ -ethoxy-4-hydroxy-3-methoxy-5 $\beta$ ,17-dimethylmorphinan-6-one, 14 $\beta$ -ethoxy-3,4-dimethoxy-5 $\beta$ ,17-dimethylmorphinan-6-one, 14 $\beta$ -benzyloxy-3,4-dimethoxy-5 $\beta$ ,17-dimethylmorphinan-6-one, 4,5 $\alpha$ -epoxy-3-hydroxy-17,17-dimethyl-6-oxo-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, (17S)-4,5 $\alpha$ -epoxy-17-ethyl-3-hydroxy-17-methyl-6-oxo-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, (17R)-4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-6-oxo-14 $\beta$ -[(3-phenylpropyl)oxy]-17-[(2(R,S)-tetrahydrofuran-2-yl)methyl]morphinan-6-one, (17R)-17-allyl-4,5 $\alpha$ -epoxy-14 $\beta$ -ethoxy-3-hydroxy-17-methyl-6-oxomorphinan-6-one, (17R)-17-allyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -methoxy-17-methyl-6-oxomorphinan-6-one, (17S)-17-allyl-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -methoxy-17-methyl-6-oxomorphinan-6-one, 4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -methoxy-17,17-dimethyl-6-oxo-morphinan-6-one, 5 $\beta$ -benzyl-14 $\beta$ -(butoxy)-4,5-epoxy-3-hydroxy-17,17-dimethyl-6-oxomorphinan-6-one, (17S)-17-allyl-5 $\beta$ -benzyl-14 $\beta$ -butoxy-4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-6-oxomorphinan-6-one, 14 $\beta$ -butoxy-4,5 $\alpha$ -epoxy-3-hydroxy-17,17-dimethyl-6-oxomorphinan-6-one, (17R)-17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-6-oxo-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, (17R)-17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-methoxy-17-methyl-6-oxo-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, (17R)-17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-6-oxo-14 $\beta$ -[(2-phenylbenzyl)oxy]morphinan-6-one, (17R)-14 $\beta$ -[(4-chlorobenzyl)oxy]-17-cyclopropylmethyl-4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-6-oxomorphinan-6-one, (17R)-4,5 $\alpha$ -epoxy-3-hydroxy-14 $\beta$ -methoxy-17-methyl-6-oxo-17-(2-phenylethyl)morphinan-6-one, 4,5 $\alpha$ -epoxy-3-methoxy-17-methyl-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one, 4,5 $\alpha$ -epoxy-3-methoxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,

4,5 $\alpha$ -epoxy-3-hydroxy-17-methyl-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,  
 4,5 $\alpha$ -epoxy-17-methyl-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,  
 17-(cyclopropylmethyl)-4,5 $\alpha$ -epoxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,  
 4,5 $\alpha$ -epoxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,  
 17-(cyclopropylmethyl)-4-hydroxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,  
 17-(cyclopropylmethyl)-4-methoxy-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,  
 4-(n-butyloxy)-17-(cyclopropylmethyl)-14 $\beta$ -[(3-phenylpropyl)oxy]morphinan-6-one,

or any pharmaceutically acceptable salt or easily accessible derivative of it.

6. Composition, comprising a compound of Claims 1 to 5 and/or a pharmaceutically acceptable acid addition salt of it, together with a pharmaceutically acceptable carrier substance.
7. Compound according to any of Claims 1 to 6 as medicament.
8. Use of a compound of Claims 1 to 5 for the manufacture of a medicament for the treatment of pain, including chronic and acute pain, post-operative pain, rheumatic diseases (e.g. arthritis), ileus, obstipation, overweight, addiction, including opioid, cocaine and alcohol addiction as well as for the manufacture of a narcotic.
9. Compounds according to Claim 1 or 2, wherein X is oxygen.
10. Compounds according to Claim 1, 2 or 9, wherein R<sub>5</sub> is OH or alkoxy.
11. Compounds according to Claim 1, 2, 9 or 10, wherein R<sub>3</sub> is hydrogen, alkyl or aralkyl, preferably hydrogen or alkyl.
12. Compounds according to Claim 1, 2, 9, 10 or 11, wherein R<sub>4</sub> is OH, alkoxy or alkenyloxy or alkynyloxy.
13. Compounds according to Claim 1, 2, 9, 10, 11 or 12, wherein a single bond is present between the carbon atoms of the numbers 7 and 8.
14. Compounds according to Claim 1, 2, 9, 10, 11, 12 or 13, wherein R<sub>2</sub> is hydrogen, alkyl or aralkyl, preferably aralkyl.

15. Compounds according to Claim 1, 2, 9, 10, 11, 12, 13 or 14, wherein R<sub>1</sub> is alkyl, (cyclical saturated group)alkyl, aralkyl or alkenyl.

16. Compounds according to Claim 1 or 2, wherein R<sub>1</sub> is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyl, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyl, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyl, where alkinyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>7</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinyl is C<sub>2</sub>-C<sub>6</sub>-alkinyl.

17. Compounds according to Claim 1, wherein R<sub>2</sub> is C<sub>4</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyl, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyl, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyl, where alkinyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>8</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinyl is C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>6</sub>-alkenoyl; C<sub>3</sub>-C<sub>6</sub>-alkinoyl; C<sub>9</sub>-C<sub>16</sub>-arylalkenoyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenoyl is C<sub>3</sub>-C<sub>6</sub>-alkenoyl; C<sub>9</sub>-C<sub>16</sub>-arylalkinoyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinoyl is C<sub>3</sub>-C<sub>6</sub>-alkinoyl.

18. Compounds according to Claim 2, wherein R<sub>2</sub> is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>16</sub>-(cyclical saturated group)alkyl, where alkyl is C<sub>1</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkenyl, where alkenyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>4</sub>-C<sub>16</sub>-(cyclical saturated group)alkinyl, where alkinyl is C<sub>2</sub>-C<sub>6</sub>; C<sub>6</sub>-C<sub>16</sub>-arylalkyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkyl is C<sub>1</sub>-C<sub>6</sub>-alkyl; C<sub>8</sub>-C<sub>16</sub>-arylalkenyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenyl is C<sub>2</sub>-C<sub>6</sub>-alkenyl; C<sub>8</sub>-C<sub>16</sub>-arylalkinyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinyl is C<sub>2</sub>-C<sub>6</sub>-alkinyl; C<sub>3</sub>-C<sub>6</sub>-alkenoyl; C<sub>3</sub>-C<sub>6</sub>-alkinoyl; C<sub>9</sub>-C<sub>16</sub>-arylalkenoyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkenoyl is C<sub>3</sub>-C<sub>6</sub>-alkenoyl; C<sub>9</sub>-C<sub>16</sub>-arylalkinoyl, where aryl is C<sub>6</sub>-C<sub>10</sub>-aryl and alkinoyl is C<sub>3</sub>-C<sub>6</sub>-alkinoyl.



## Morphinanderivate und deren quartäre Ammoniumsalze substituiert in Position 14, Herstellungsverfahren und Verwendung

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Die vorliegende Erfindung betrifft eine Klasse von Morphinanverbindungen und deren quartäre Ammoniumsalze substituiert in Position 14, die als hochaktive Analgetika aber auch als Opioidantagonisten verwendet werden können. Die vorliegende Erfindung bezieht sich auch auf deren pharmazeutisch akzeptierbaren Salze und leicht zugänglichen Derivate, auf einen Prozess zu deren Herstellung und deren Verwendung in der Herstellung pharmazeutischer Spezialitäten.

Die Existenz von Opioid-Rezeptoren als Rezeptoren des Zentralnervensystems (ZNS), welche analgetische Wirkung vermitteln, ist eindeutig erwiesen. Diese Rezeptoren werden in drei Subtypen,  $\mu$ ,  $\kappa$  und  $\delta$  eingeteilt. Aktivierung dieser Rezeptoren durch Opioidagonisten hat einen analgetischen Effekt zur Folge. Die Aktivierung der  $\mu$ -Rezeptoren bewirkt den höchsten analgetischen Effekt, wobei besonders N-methylsubstituierte Morphinane mit einer Sauerstofffunktion in Position 6 (Morphin, Oxymorphon, Hydromorphon etc.) besonders aktive Opioidagonisten sind und als effektive Analgetika eingesetzt werden. In der Vergangenheit wurde viel Arbeit in Struktur-Aktivitäts-Beziehungsstudien dieser Substanzklasse investiert.

Im Journal of Medicinal Chemistry 1984, 27, S. 1575-1579 sind verschiedene 14-Methoxy-N-methylmorphinan-6-one mit verschiedenen Substituenten in Position 3 beschrieben. Diese Derivate zeigen höhere analgetische Aktivität als deren 14-Hydroxyanaloga.

Eine detaillierte Studie von 5-Methyloxymorphon (= 14-Hydroxy-5-methyldihydromorphinon) ist in Helvetica Chimica Acta (1988, 71, S. 1801-1804) beschrieben, die zu dem Ergebnis gelangt, daß die Einführung einer 5-Methylgruppe die opioidagonistischen Eigenschaften von Oxymorphon verringert.

Eine weitere Studie an 14-Alkoxy-N-methylmorphinan-6-onen ist in Helvetica Chimica Acta 1989, 72, S. 1233-1239 beschrieben, in welcher der Einfluß verschiedener Substituenten in Position 3 und des Aminstickstoffs evaluiert wurden.